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L3: Entry 4 of 4

File: USPT

Nov 16, 1999

US-PAT-NO: 5986051

DOCUMENT-IDENTIFIER: US 5986051 A

TITLE: Genes of Helicobacter pylori necessary for the regulation and maturation of urease and their use

DATE-ISSUED: November 16, 1999

## INVENTOR-INFORMATION:

| NAME             | CITY             | STATE | ZIP CODE | COUNTRY |
|------------------|------------------|-------|----------|---------|
| Labigne; Agnes   | Bures Sur Yvette |       |          | FR      |
| Cussac; Valerie  | Paris            |       |          | FR      |
| Ferrero; Richard | Paris            |       |          | FR      |

## ASSIGNEE-INFORMATION:

| NAME  | CITY  | STATE | ZIP CODE | COUNTRY | TYPE | CODE |
|---|-------|-------|----------|---------|------|------|
| Institut Pasteur  | Paris |       |          | FR      |      | 03   |
| Institut National de la Santa et de la Recherche Medicale | Paris |       |          | FR      |      | 03   |

APPL-NO: 08/ 211312   [PALM]

DATE FILED: July 1, 1994

## FOREIGN-APPL-PRIORITY-DATA:

| COUNTRY | APPL-NO  | APPL-DATE       |
|---------|----------|-----------------|
| FR      | 91 12198 | October 3, 1991 |

## PCT-DATA:

| APPL-NO        | DATE-FILED      | PUB-NO     | PUB-DATE     | 371-DATE    | 102 (E) -DATE |
|----------------|-----------------|------------|--------------|-------------|---------------|
| PCT/FR92/00921 | October 2, 1992 | WO93/07273 | Apr 15, 1993 | Jul 1, 1994 | Jul 1, 1994   |

INT-CL: [06] C07 K 1/00, C07 K 16/00, A61 K 38/00, A61 K 38/04

US-CL-ISSUED: 530/350; 530/300, 530/328, 530/388.1, 530/387.1, 530/389.5

US-CL-CURRENT: 530/350; 530/300, 530/328, 530/387.1, 530/388.1, 530/389.5

FIELD-OF-SEARCH: 530/300, 530/350, 530/328, 530/388.1, 530/387.1, 530/389.5

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

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|                          | PAT-NO         | ISSUE-DATE    | PATENTEE-NAME     | US-CL  |
|--------------------------|----------------|---------------|-------------------|--------|
| <input type="checkbox"/> | <u>4785086</u> | November 1988 | Rashtchian et al. | 536/27 |
| <input type="checkbox"/> | <u>5459041</u> | October 1995  | Blaser et al.     |        |
| <input type="checkbox"/> | <u>5498528</u> | March 1996    | King              |        |
| <input type="checkbox"/> | <u>5538729</u> | July 1996     | Czinn et al.      |        |
| <input type="checkbox"/> | <u>5601848</u> | February 1997 | Marshall          |        |

## FOREIGN PATENT DOCUMENTS

| FOREIGN-PAT-NO | PUBN-DATE     | COUNTRY | US-CL |
|----------------|---------------|---------|-------|
| A 0367 644     | May 1990      | EP      |       |
| 0 745 674      | May 1996      | EP      |       |
| 90 04030       | April 1990    | WO      |       |
| WO 91 09049    | June 1991     | WO      |       |
| WO 96/33732    | October 1996  | WO      |       |
| WO 96/40893    | December 1996 | WO      |       |
| WO 96/38475    | December 1996 | WO      |       |

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V. Cussac et al., "Expression of Helicobacter pylori Urease Genes in Escherichia coli Grown Under Nitrogen-Limiting Conditions", J. Bacteriology 174(8):2466-2473 (Apr. 1992).  
R. Ferrero et al., "Construction of Urease Deficient Mutants of Helicobacter pylori By Allelic Exchange", Society for Microbial Ecology and Disease, vol. 4(S), Oct. 1991, p. S136, Abstract H4-1.  
T. Sugiyama et al., "A Novel Enzyme Immunoassay for Serodiagnosis of Helicobacter pylori Infection", Gastroenterology 101:77-83 (1991).

ART-UNIT: 165

PRIMARY-EXAMINER: Minnifield; Nita

ATTY-AGENT-FIRM: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

ABSTRACT:

This invention relates to Helicobacter polypeptides, particularly UreE, UreF, UreG, UreH, and UreI, immunogenic fragments of those polypeptides, and compositions containing those polypeptides or fragments. This invention also relates to purified antibodies that bind to the polypeptides of this invention and to compositions comprising those antibodies.

16 Claims, 24 Drawing figures

13793169 PMID: 9492267

**Characterisation of a binding-protein-dependent, active transport system for short-chain amides and urea in the methylotrophic bacterium *Methylophilus methylotrophus*.**

Mills J; Wyborn N R; Greenwood J A; Williams S G; Jones C W  
Department of Biochemistry, University of Leicester, England.

European journal of biochemistry / FEBS (GERMANY) Jan 15 1998, 251  
(1-2) p45-53, ISSN 0014-2956 Journal Code: 0107600

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Three genes (fmdCAB) encoding an outer-membrane porin for short-chain amides and urea, formamidase, and a putative regulatory protein in *Methylophilus methylotrophus* have previously been cloned and characterised. Three genes have now been identified downstream of fmdB, viz fmdD encoding a hydrophilic protein containing an N-terminal signal sequence, and fmdEF encoding hydrophobic transmembrane proteins. The derived amino acid sequence of mature FmdD (predicted molecular mass 41,870 Da) was similar to the cytoplasmic, amide-binding protein (AmiC) from *Pseudomonas aeruginosa* and to several periplasmic, solute-binding proteins from other **bacteria**. Mature FmdD was purified and shown to be a monomer (40-45 kDa) with the predicted N-terminal amino acid sequence (ADYPTA-). Equilibrium dialysis showed that the purified protein bound short-chain amides and urea with high affinity (Kd 7.2 microm for [14C]urea). SDS/PAGE and western blotting using antiserum to mature FmdD showed it was induced by short-chain amides and urea, and repressed by excess ammonia. The derived amino acid sequences of FmdE (32,822 Da) and FmdF (incomplete; >25,435 Da) were similar to the transmembrane proteins BraD/LivH and BraE/LivM, respectively, in various leucine/isoleucine/valine transport systems. Uptake of [14C]urea by washed cells was **inhibited** by the uncoupling agent carbonyl cyanide p-trifluoromethoxyphenylhydrazone and unlabelled formamide. It is concluded that FmdDEF comprise part of a high-affinity, binding-protein-dependent active-**transport** system for short-chain **amides** and urea in *M. methylotrophus*.

Tags: Support, Non-U.S. Gov't

Descriptors: Amides--metabolism--ME; \* **Bacterial** Proteins--genetics--GE; \* **Bacterial** Proteins--metabolism--ME; \*Gram-Negative Aerobic Rods and Cocci--chemistry--CH; \*Membrane Proteins--genetics--GE; \*Membrane Proteins--metabolism--ME; \*Periplasmic Binding Proteins; \*Porins--genetics--GE; \*Porins--metabolism--ME; \*Urea--metabolism--ME; Amino Acid Sequence; **Bacterial** Proteins--chemistry--CH; Base Sequence; Biological Transport; Gene Expression Regulation, **Bacterial**; Gram-Negative Aerobic Rods and Cocci--genetics--GE; Gram-Negative Aerobic Rods and Cocci--metabolism--ME; Membrane Proteins--chemistry--CH; Molecular Sequence Data; Sequence Analysis; Sequence Homology, Amino Acid

Molecular Sequence Databank No.: GENBANK/Y14964

CAS Registry No.: 0 (Amides); 0 (Bacterial Proteins); 0 (Membrane Proteins); 0 (Periplasmic Binding Proteins); 0 (Porins); 0 (fmdD protein); 0 (fmdE protein, *Methylophilus methylotrophus*); 0 (fmdF protein, *Methylophilus*); 142462-53-1 (AmiC protein, *Pseudomonas aeruginosa*); 57-13-6 (Urea)

Record Date Created: 19980323

Record Date Completed: 19980323

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Search Results - Record(s) 1 through 2 of 2 returned.

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L2: Entry 1 of 2

File: USPT

Apr 25, 1995

US-PAT-NO: 5409903

DOCUMENT-IDENTIFIER: US 5409903 A

TITLE: Method and compositions for the treatment of H. pylori and dermatitis

DATE-ISSUED: April 25, 1995

US-CL-CURRENT: 514/23; 424/402, 424/447, 424/449, 424/451, 424/464, 424/489,  
424/499, 514/865, 514/870, 514/925, 602/904INT-CL: [06] A61 K 9/50, A61 K 15/00, A61 K 9/26

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L2: Entry 2 of 2

File: USPT

Mar 2, 1993

US-PAT-NO: 5190961

DOCUMENT-IDENTIFIER: US 5190961 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Thiourea derivatives and antimicrobial agent and antulcer agent containing the same

DATE-ISSUED: March 2, 1993

US-CL-CURRENT: 514/331; 514/308, 514/318, 514/326, 514/343, 514/353, 514/422,  
514/428, 514/438, 514/447, 514/471, 514/472, 514/586, 546/193, 546/213, 546/214,  
546/231, 546/276.4, 546/305, 546/331, 548/517, 548/527, 548/567, 549/482, 549/496,  
549/69, 549/77, 564/17, 564/22, 564/23, 564/27INT-CL: [05] A61K 31/445, A61K 31/40, A61K 31/17, A61K 31/34, C07L 335/12, C07D  
403/10, C07D 405/10, C07D 409/10

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23619 AMIDE?

267598 TRANSPORT?

S3 95 AMIDE? (5N) TRANSPORT?

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95 S3

98400 INACTIVA?

1078760 INHIBIT?

473457 ANTAGON?

356755 BLOCK?

190838 MODULAT?

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56 S4

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S5 6 S4 AND BACTERI?

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| <input type="checkbox"/> | L2       | L1 and (treat\$ or prevent\$ or therapeut\$)      | 1         |
| <input type="checkbox"/> | L3       | labigne.in. and ((urei or ure-i) same antibod\$)  | 4         |
| <input type="checkbox"/> | L4       | ('5986051'  '6258359'  '6416968'  '6190667')!.PN. | 4         |

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Search Results - Record(s) 1 through 4 of 4 returned.

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L4: Entry 1 of 4

File: USPT

Jul 9, 2002

US-PAT-NO: 6416968

DOCUMENT-IDENTIFIER: US 6416968 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Methods of inhibiting Helicobacter pylori

DATE-ISSUED: July 9, 2002

US-CL-CURRENT: 435/32; 424/141.1, 424/150.1, 424/184.1, 424/234.1, 424/236.1,  
424/94.1, 435/106, 435/12, 435/18, 435/252.1, 435/29, 435/4, 435/6, 435/69.1,  
514/230.5, 514/44, 530/300, 530/350INT-CL: [07] C12 Q 1/18

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L4: Entry 2 of 4

File: USPT

Jul 10, 2001

US-PAT-NO: 6258359

DOCUMENT-IDENTIFIER: US 6258359 B1

**\*\* See image for Certificate of Correction \*\***TITLE: Immunogenic compositions against helicobacter infection, polypeptides for  
use in the compositions, and nucleic acid sequences encoding said polypeptides

DATE-ISSUED: July 10, 2001

US-CL-CURRENT: 424/141.1; 424/150.1, 424/163.1, 424/164.1, 530/350, 530/388.1,  
530/388.2, 530/388.4INT-CL: [07] A61 K 39/395, A61 K 39/40, C07 K 1/00, C07 K 16/00

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L4: Entry 3 of 4

File: USPT

Feb 20, 2001

US-PAT-NO: 6190667

DOCUMENT-IDENTIFIER: US 6190667 B1

TITLE: Methods of inhibiting Helicobacter pylori

DATE-ISSUED: February 20, 2001

US-CL-CURRENT: 424/234.1; 424/780, 435/32INT-CL: [07] A61 K 39/02

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L4: Entry 4 of 4

File: USPT

Nov 16, 1999

US-PAT-NO: 5986051

DOCUMENT-IDENTIFIER: US 5986051 A



TITLE: Genes of Helicobacter pylori necessary for the regulation and maturation of urease and their use

DATE-ISSUED: November 16, 1999

US-CL-CURRENT: 530/350; 530/300, 530/328, 530/387.1, 530/388.1, 530/389.5

INT-CL: [06] C07 K 1/00, C07 K 16/00, A61 K 38/00, A61 K 38/04

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- 
- ☐ 1. [6706724](#). 21 Dec 01; 16 Mar 04. Substituted aryl compounds as novel cyclooxygenase-2 selective inhibitors, compositions and methods of use. Khanapure; Subhash P., et al. 514/277; 514/336 514/340 514/342 514/365 514/374 514/443 514/469 546/1 546/114 546/115 546/208 548/146 548/152 548/153 548/217 549/229 549/396 549/398 549/430 549/462 549/469 549/472. A61K031/435 A61K031/42 C07D213/00 C07D277/04 C07D317/08.
- 
- ☐ 2. [6649629](#). 22 Dec 00; 18 Nov 03. Nitrosated and nitrosylated cyclooxygenase-2 inhibitors, compositions and methods of use. Bandarage; Upul K., et al. 514/326; 514/378 514/406 546/209 548/247 548/248 548/375.1 548/561. C07D207/325 C07D231/06 A61K031/40 A61K031/415.
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- ☐ 3. [6552047](#). 17 Nov 99; 22 Apr 03. H2 receptor antagonist compounds in combination with nitric oxide donors, compositions and methods of use. Garvey; David S., et al. 514/331; 514/365 514/370 514/398 514/400 514/471. A61K031/416.
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- ☐ 4. [6517809](#). 01 Aug 00; 11 Feb 03. Process for preparing a reactive pharmaceutical product for the detection of gastrointestinal disorder caused by bacteria in the gastrointestinal superior tract. Marshall; Barry J.. 424/1.37; 424/1.25 424/1.29 424/1.33 424/1.81. A61K051/00.
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- ☐ 5. [6379910](#). 04 Jun 98; 30 Apr 02. Measuring apparatus and method for material or organism inducing PH-change of substrate solution. Nakamura; Michihiro, et al. 435/12; 422/57 422/61 422/81 435/7.1 435/7.32 436/501 436/512. C12Q001/58.
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- ☐ 6. [6312918](#). 18 Apr 95; 06 Nov 01. Examination method of infection with Helicobacter pylori. Ito; Masaharu, et al. 435/34; 435/12. C12Q001/04.
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- ☐ 7. [6258359](#). 06 Jun 95; 10 Jul 01. Immunogenic compositions against helicobacter infection, polypeptides for use in the compositions, and nucleic acid sequences encoding said polypeptides. Labigne; Agnes, et al. 424/141.1; 424/150.1 424/163.1 424/164.1 530/350 530/388.1 530/388.2 530/388.4. A61K039/395 A61K039/40 C07K001/00 C07K016/00.
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- ☐ 8. [6228605](#). 26 Mar 97; 08 May 01. Detection of helicobacter pylori in the stomach. Marshall; Barry J.. 435/34; 435/12. C12Q001/04.
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- ☐ 9. [6190667](#). 30 Jun 98; 20 Feb 01. Methods of inhibiting Helicobacter pylori. De Reuse; Hilde, et al. 424/234.1; 424/780 435/32. A61K039/02.
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- ☐ 10. [6187556](#). 02 Dec 99; 13 Feb 01. Composition, kit, and method for detecting Helicobacter pylori in biopsy. Lee; Jong-Hwa, et al. 435/34; 435/12 435/975. C12Q001/04 C12Q001/58 G01N033/53.
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- ☐ 12. [6149908](#). 22 Jul 98; 21 Nov 00. Use of lactoperoxidase, a peroxide donor and thiocyanate for the manufacture of a medicament for treating Helicobacter pylori infection. Claesson; Carl Olof, et al.
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424/94.4;. A61K038/44.

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13. 6083756. 07 May 98; 04 Jul 00. Prevention of sudden infant death. Hedner; Jan, et al. 436/63; 422/83 422/84 435/7.92 436/513 436/900 600/300 600/532 600/543. G01N033/48 A61B005/08.

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14. 6067989. 26 Feb 97; 30 May 00. Breath test for the diagnosis of Helicobacter pylori infection in the gastrointestinal tract. Katzman; Daniel E.. 128/898; 422/84 600/532 73/23.3. A61B019/00 C07C002/02.

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15. 6027878. 07 Jun 95; 22 Feb 00. Genes of Helicobacter pylori necessary for the regulation and maturation of urease and their use. Labigne; Agnes, et al. 435/6; 435/252.3 435/252.33 435/320.1 435/91.2 536/22.1 536/23.1 536/24.3 536/24.31 536/24.32 536/24.33. C12Q001/68 C12P019/34 C07H021/02 C07H021/04.

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16. 5955054. 29 Apr 98; 21 Sep 99. Diagnostic assay for localizing H. pylori. Hartmann; John F.. 424/1.65; 424/1.11 424/9.1 424/9.4. A61K051/00 A61M036/14.

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17. 5942409. 31 Jul 98; 24 Aug 99. Process for identification of substances modulating ureI dependent mechanisms of Helicobacter pylori metabolism. Sachs; George, et al. 435/32; 435/12 435/29 435/4. C12Q001/18 C12Q001/58 C12Q001/02 C12Q001/00.

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18. 5900410. 12 Aug 97; 04 May 99. Monotherapy of peptic ulcers and gastritis. Hartmann; John F.. 514/81; 514/82 544/337. A61K031/675 C07F009/6561 C07F009/6558.

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20. 5854013. 19 May 97; 29 Dec 98. Method of determining the presence or absence of a nonparaffinophilic microorganism in a specimen. Ollar; Robert-A., et al. 435/34; 435/248 435/30. C12Q001/04.

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21. 5848975. 29 Sep 97; 15 Dec 98. Breath test for helicobacter pylori. Phillips; Michael. 600/532; 128/898 600/300 600/543. A61B005/08.

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22. 5542419. 28 Feb 94; 06 Aug 96. Noninvasive method to detect gastric Helicobacter pylori. Moulton-Barrett; Rex, et al. 600/366; 600/573. A61B005/08.

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23. 5514660. 07 Jun 95; 07 May 96. Method for treating and inhibiting gastric and duodenal ulcers. Zopf; David A., et al. 514/25; 514/24 514/42 514/53 514/54 514/61 536/18.7 536/22.1 536/4.1. A61K031/715 A61K031/73.

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24. 5507289. 23 Mar 94; 16 Apr 96. System and method to diagnose bacterial growth. Essen-Moller; Anders. 600/348; 600/301. A61B005/00.

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25. 5498528. 10 Jun 94; 12 Mar 96. Detection of helicobacter pylori. King; Wing. 435/34; 435/29 435/4 435/810 436/63 436/74. C12Q001/04 C12Q001/02 G01N033/48 G01N033/20.

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26. 5409903. 18 Feb 92; 25 Apr 95. Method and compositions for the treatment of H. pylori and dermatitis. Polak; Robert B., et al. 514/23; 424/402 424/447 424/449 424/451 424/464 424/489 424/499 514/865 514/870 514/925 602/904. A61K009/50 A61K015/00 A61K009/26.

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☐ 27. 5214053. 02 Sep 92; 25 May 93. Thiourea derivatives and antimicrobial agent and antiulcer agent containing the same. Nakazawa; Keiichi, et al. 514/318; 514/321 514/452 514/464 546/194 546/197 549/362 549/365. C07D211/06.

☐ 28. 5190961. 02 Aug 91; 02 Mar 93. Thiourea derivatives and antimicrobial agent and antiulcer agent containing the same. Hasegawa; Hirokazu, et al. 514/331; 514/308 514/318 514/326 514/343 514/353 514/422 514/428 514/438 514/447 514/471 514/472 514/586 546/193 546/213 546/214 546/231 546/276.4 546/305 546/331 548/517 548/527 548/567 549/482 549/496 549/69 549/77 564/17 564/22 564/23 564/27. A61K031/445 A61K031/40 A61K031/17 A61K031/34 C07L335/12 C07D403/10 C07D405/10 C07D409/10.

☐ 29. 4947861. 01 May 89; 14 Aug 90. Noninvasive diagnosis of gastritis and duodenitis. Hamilton; Lyle H.. 600/532; 128/898 600/543. A61O005/08.

☐ 30. 4923801. 13 Apr 87; 08 May 90. Compositions and methods for the enrichment and isolation of *Campylobacter pylori* and related organisms from biological specimens and the environment. Marshall; Barry J., et al. 435/12; 435/18 435/252.1 435/30 435/34. C12Q001/58 C12Q001/04 C12Q001/34 C12Q001/24.

☐ 31. 4830010. 22 Jan 88; 16 May 89. Methods for the diagnosis of gastrointestinal disorders. Marshall; Barry J.. 600/300; 436/811 600/532. A61B005/00.

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| <input type="checkbox"/> | L2              | urca near2 channel               | 27               |

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